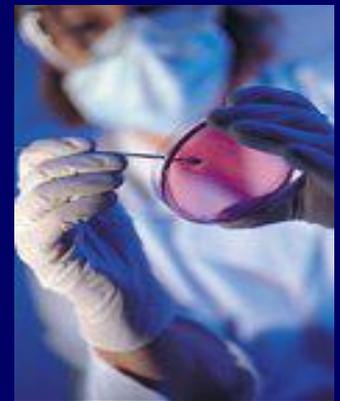
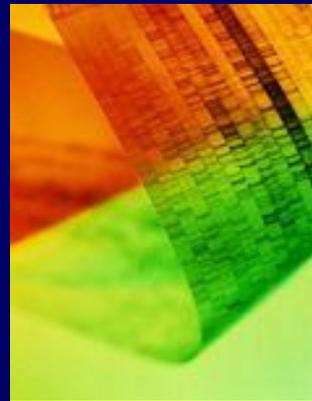


# H5N1 Avian Influenza Virus Manuscripts and Dual Use Research Concerns:

U.S. National Science Advisory Board for Biosecurity



**Joseph Kanabrocki, Ph.D., C.B.S.P.**

*The University of Chicago*

**African Biological Safety Association**

Johannesburg, South Africa

June 25, 2012

# Issue (Oct 2011)



- **Two US government-funded studies on respiratory transmission of H5N1 were submitted for publication**
- **The manuscripts raise “dual use research concerns” in that they contain information that could be utilized to create a potentially human-transmissible form of H5N1 that could be intentionally released to threaten public health and security**
- **In recognition of this, the US government tasked the NSABB with reviewing the unpublished manuscripts and making recommendations on their communication.**

# What is the NSABB?



- **National Science Advisory Board for Biosecurity**
- **Committee of subject matter experts**
- **Advises the US government on how to minimize the risk that information, products, and technology from life sciences research could be misused to cause harm to public health and safety, agriculture, plants, animals, the environment, or materiel**
- **For more information on NSABB and its reports:**  
**[www.biosecurityboard.gov](http://www.biosecurityboard.gov)**

# NSABB Approach (Oct 2011)



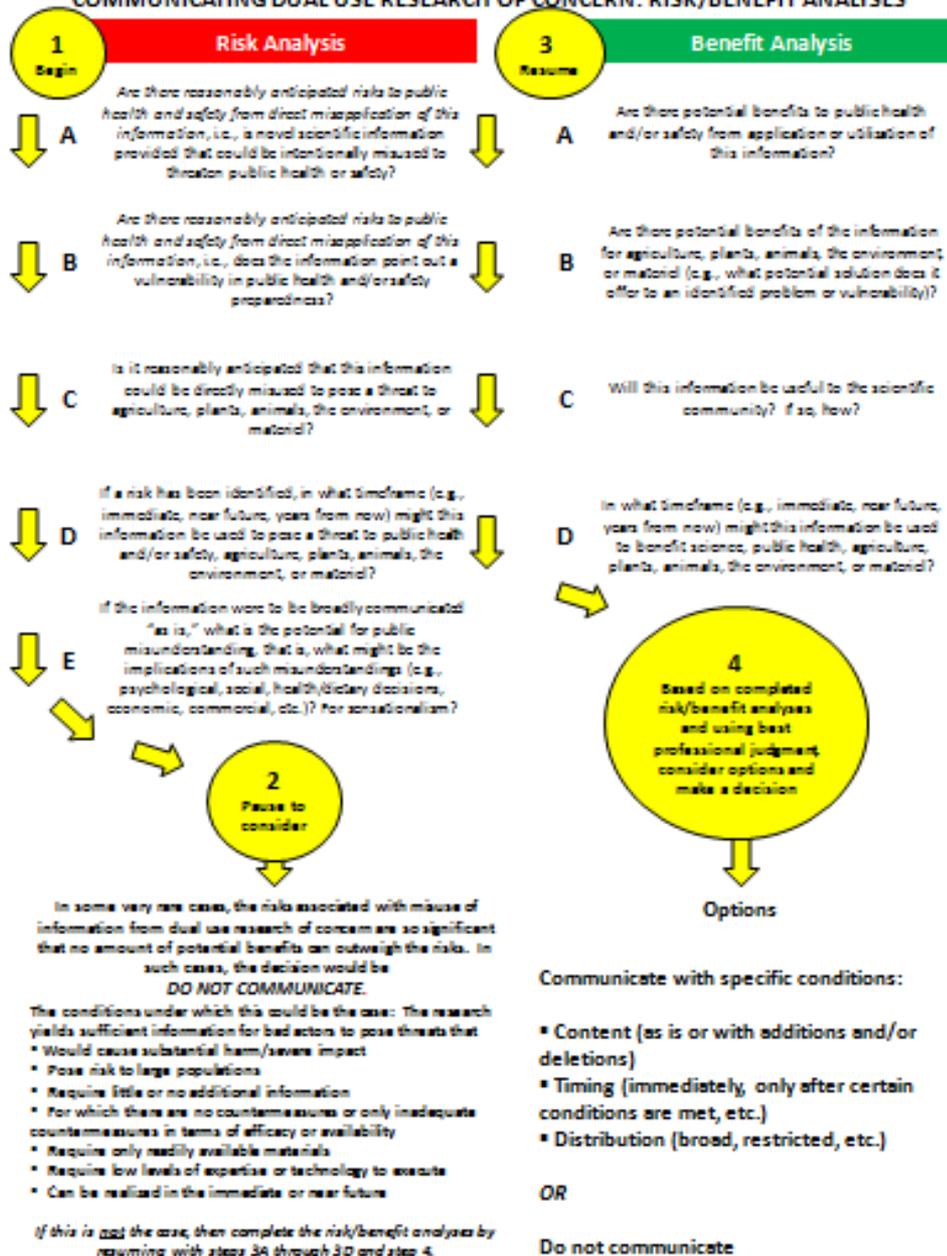
- **NSABB Working Group established to:**
  - Assess the dual use research implications
  - Consider the risks and benefits of communicating the research
  - Provide draft findings and recommendations to the full NSABB
  
- **NSABB Working Group included:**
  - Subset of NSABB voting members
  - US Federal agency representatives – ex officio members
  - Outside subject matter experts

# NSABB Approach (Oct 2011)



- **NSABB Working Group Deliberations**
  - In-depth review and discussion of the manuscripts
    - Q&A with PIs
    - Utilized NSABB communication tool as a framework for the risk and benefit analysis of communicating the information in the manuscripts
  - Developed draft recommendations for full NSABB consideration
- **NSABB Deliberations**
  - In closed sessions due to discussion of unpublished information
  - Issued findings and recommendations to US Government

COMMUNICATING DUAL USE RESEARCH OF CONCERN: RISK/BENEFIT ANALYSES



# Communicating Dual Use Research of Concern: A Process Map for Risk/Benefit Analyses

**1  
Begin**

# Risk Analysis

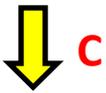
*Are there reasonably anticipated risks to public health and safety from direct misapplication of this information, i.e., is novel scientific information provided that could be intentionally misused to threaten public health or safety?*



*Are there reasonably anticipated risks to public health and safety from direct misapplication of this information, i.e., does the information point out a vulnerability in public health and/or safety preparedness?*



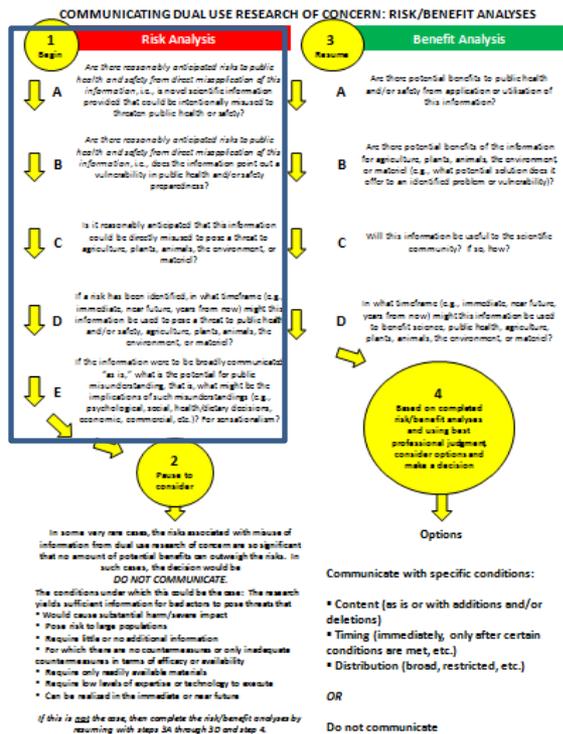
*Is it reasonably anticipated that this information could be directly misused to pose a threat to agriculture, plants, animals, the environment, or materiel?*

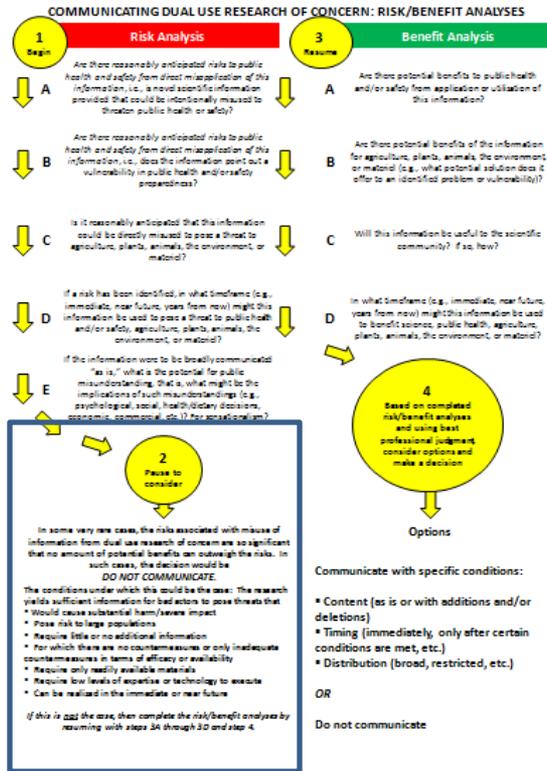
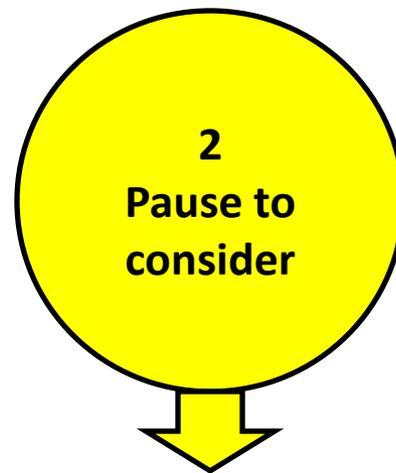


*If a risk has been identified, in what timeframe (e.g., immediate, near future, years from now) might this information be used to pose a threat to public health and/or safety, agriculture, plants, animals, the environment, or materiel?*



*If the information were to be broadly communicated “as is,” what is the potential for public misunderstanding, that is, what might be the implications of such misunderstandings (e.g., psychological, social, health/dietary decisions, economic, commercial, etc.)? For sensationalism?*





In some very rare cases, the risks associated with misuse of information from dual use research of concern are so significant that no amount of potential benefits can outweigh the risks. In such cases, the decision would be **DO NOT COMMUNICATE**.

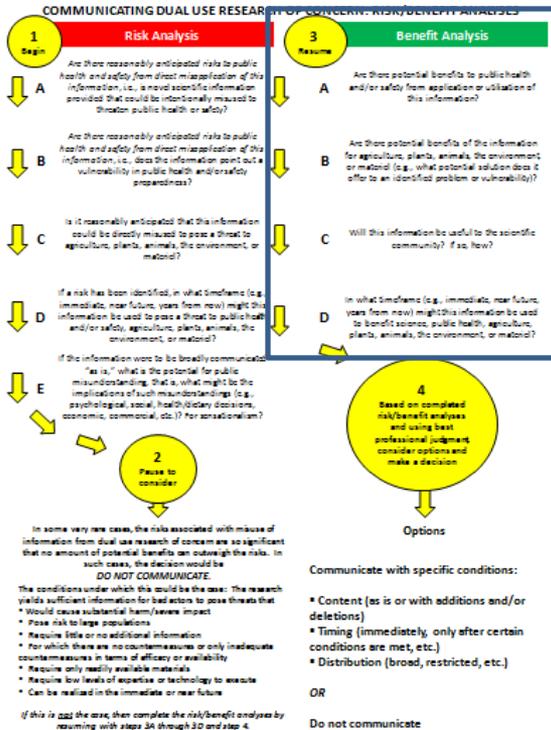
The conditions under which this could be the case: The research yields sufficient information for bad actors to pose threats that

- Would cause substantial harm/severe impact
- Pose risk to large populations
- Require little or no additional information
- For which there are no countermeasures or only inadequate countermeasures in terms of efficacy or availability
- Require only readily available materials
- Require low levels of expertise or technology to execute
- Can be realized in the immediate or near future

If this is not the case, then complete the risk/benefit analyses by resuming with steps 3A through 3D and step 4.

### 3 Resume

# Benefit Analysis



**A**

Are there potential benefits to public health and/or safety from application or utilization of this information?



**B**

Are there potential benefits of the information for agriculture, plants, animals, the environment, or material (e.g., what potential solution does it offer to an identified problem or vulnerability)?



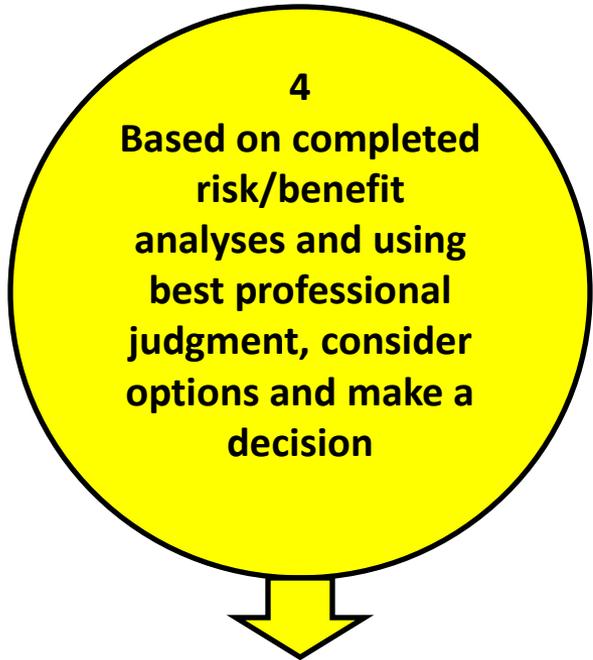
**C**

Will this information be useful to the scientific community? If so, how?



**D**

In what timeframe (e.g., immediate, near future, years from now) might this information be used to benefit science, public health, agriculture, plants, animals, the environment, or material?



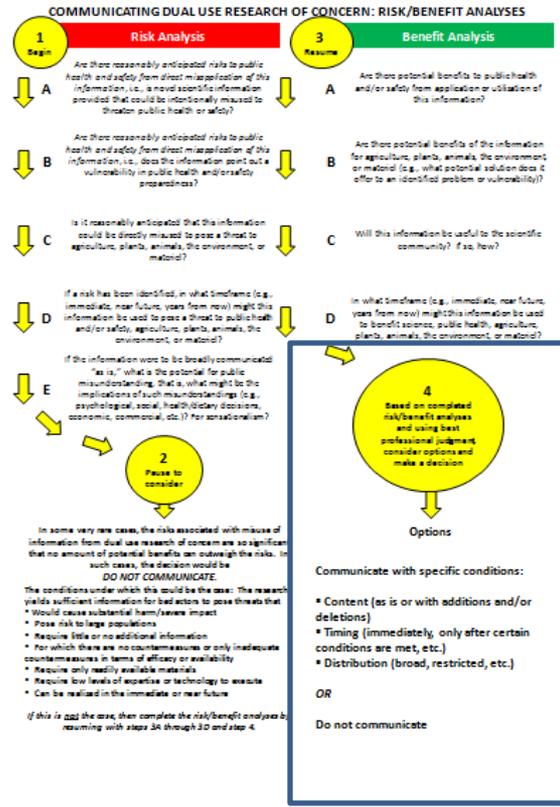
Options

**Communicate with specific conditions:**

- Content (as is or with additions and/or deletions)
  - Timing (immediately, only after certain conditions are met, etc.)
  - Distribution (broad, restricted, etc.)
- OR

OR

Do not communicate



# NSABB Recommendations (Nov 2011)



- The Board unanimously recommended that neither manuscript be published with complete data and experimental details.
- The Board further recommended that:
  - The conclusions of the manuscripts be published, but without experimental details and mutation data that would enable replication of the experiments.
  - Text be added describing:
    - the goals of the research
    - the potential benefits to public health (including informing surveillance efforts, pandemic preparedness activities, and countermeasure development and stockpiling efforts)
    - the risk assessments performed prior to research initiation
    - the ongoing biosafety oversight, containment, and occupational health measures
    - biosecurity practices and adherence to select agent regulation
    - that addressing biosafety, biosecurity, and occupational health is part of the responsible conduct of all life sciences research.

# NSABB Recommendations (Nov 2011)



- The Board also recommended that:
  - The NSABB develop a statement that explains their review process and rationale for the recommendations. This statement will be provided to the journals to consider for publication.\*
  - The USG encourage the authors to submit a special communication/commentary letter to the journals regarding the dual use research issue.

*Start a Global Conversation*

\* *Nature* (2012) doi:10.1038/482153a and *Science* (2012) doi:10.1126/science.1217994  
<http://www.nature.com/nature/journal/vaop/ncurrent/full/482153a.html>  
<http://www.sciencemag.org/content/335/6069/660>

# NSABB Rationale (Nov 2011)



- If influenza A/H5N1 virus acquires the capacity for human-to-human spread and retained its current virulence, the world could face an pandemic of significant proportions.
- Before these experiments were done, it was uncertain whether avian influenza A/H5N1 could ever acquire the capacity for mammal-to-mammal transmission. Now that this information is known, society can take steps globally to prepare for when nature might generate such a virus spontaneously.

\* *Nature* (2012) doi:10.1038/482153a and *Science* (2012) doi:10.1126/science.1217994  
<http://www.nature.com/nature/journal/vaop/ncurrent/full/482153a.html>  
<http://www.sciencemag.org/content/335/6069/660>

# NSABB Rationale (Nov 2011)



- At the same time, these scientific results also represent a grave concern for global biosecurity, biosafety, and public health. Could this knowledge, in the hands of malevolent individuals, organizations or governments, allow construction of a genetically altered influenza virus capable of causing a pandemic with mortality exceeding that of the 1918 'Spanish flu' epidemic?
- The NSABB found the potential risk of public harm to be of unusually high magnitude.
- In formulating the recommendations, the NSABB tried to balance the great risks against the benefits that could come from making the details of this research known.
- Because the NSABB found that there was significant potential for harm in fully publishing these results and that the harm exceeded the benefits of publication, the Board therefore recommended that the work not be fully communicated in an open forum.

# NSABB Deliberations (March 2012)



- Two day Face-to-Face meeting
- Authors, Editors, Subject Area Experts, Security Briefing, Funding Agency
- Papers under *Export Controls*

# NSABB Recommendations (March 2012)



- “Kawaoka” paper
  - Unanimous support for publication of this paper.
- “Fouchier” paper
  - 12:6 vote in favor of publish the methods, results and conclusions of this paper.

[http://oba.od.nih.gov/oba/biosecurity/PDF/NSABB\\_Statement\\_March\\_2012\\_Meeting.pdf](http://oba.od.nih.gov/oba/biosecurity/PDF/NSABB_Statement_March_2012_Meeting.pdf)

# What was different?



- NSABB reviewed revised manuscripts with more clarity on the risks and benefits.
- NSABB received additional non-public information on both the benefits and the risks.
- The USG issued new policy guidelines and continues to revise oversight programs.
- The lack of a restricted data distribution mechanism.

# New USG Policy on DURC



## High Consequence DURC Research

- [http://oba.od.nih.gov/oba/biosecurity/PDF/United States Government Policy for Oversight of DURC FINAL version 032812.pdf](http://oba.od.nih.gov/oba/biosecurity/PDF/United%20States%20Government%20Policy%20for%20Oversight%20of%20DURC%20FINAL%20version%20032812.pdf)

# New USG Policy on DURC



## ■ Tier 1 Select Agents + H5N1 (HPAI)

<b><i>Francisella tularensis</i></b>	<b>Ebola virus</b>
<b><i>Yersinia pestis</i></b>	<b>Marburg virus</b>
<b><i>Bacillus anthracis</i></b>	<b>Variola major virus</b>
<b><i>Burkholderia mallei</i></b>	<b>Variola minor virus</b>
<b><i>Burkholderia pseudomallei</i></b>	Influenza A H5N1 (HPAI)
<b>Toxin-producing strains of <i>Clostridium botulinum</i></b>	<b>Botulinum neurotoxin</b>

# Seven Experiments of Concern



- Enhance the harmful consequences of a biological agent or toxin.
- Disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification.
- Confer resistance to prophylactic or therapeutic interventions or facilitate their ability to evade detection methodologies.

# Seven Experiments of Concern



- Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin.
- Alter the host range or tropism of a biological agent or toxin.
- Enhance the susceptibility of a host population.
- Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.

# What next?



- Promote Meaningful International Scientific and Policy Dialog
- New USG DURC Policy announced. Other countries will likely also announce policies.
- WHO will convene a meeting in Fall 2012
- Is this another Asilomar moment?